

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: De Francesco et al.

Serial No.: 08/952,981 Case No.: IT0002PCA

Filed:

For: METHOD FOR REPRODUCING IN
VITRO THE RNA-DEPENDENT RNA
POLYMERASE AND TERMINAL
NUCLEOTIDYL TRANSFERASE
ACTIVITIES ENCODED BY
HEPATITIS C VIRUS (HCV)

Art Unit:

Examiner:

EXPRESS MAIL CERTIFICATE
DATE OF DEPOSIT Feb 27, 2002
EXPRESS MAIL NO. EL52391158748
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS
BEING DEPOSITED WITH THE UNITED STATES POSTAL
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MAILED BY Christine C. [Signature]
DATE 2-27-02

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the enclosed application as provided below.

In the Specification:

Please amend the specification by inserting before the first sentence:

-- The present application is a continuation of U.S. Application No. 08/952,981, filed
March 23, 1998, which is the U.S national filing of PCT/IT96/00106, International filing date
May 24, 1996 (published in English).--

Please amend the specification by replacing the Sequence Listing with the enclosed
Sequence Listing.

In the Claims:

Please cancel claims 2-7 without prejudice to future prosecution. Please add the
following claims:

8. (New) A method for producing *in vitro* the RNA-dependent RNA polymerase activity encoded by hepatitis C virus (HCV), comprising the step of incubating together HCV NS5B, ribonucleotide substrates, and a RNA template, under conditions suitable to produce said RNA-dependent RNA polymerase activity, provided that said incubating takes place *in vitro*.

9. (New) The method of claim 8, wherein said NS5B is purified.

10. (New) The method of claim 9, wherein said NS5B has the amino acid sequence of SEQ ID NO:1.

11. (New) The method of claim 8, wherein said NS5B is produced from a NS2-NS3-NS4-NS5 polyprotein by means of multiple proteolytic events that occur in an organism expressing nucleic acid encoding said NS2-NS3-NS4-NS5 polyprotein, followed by purification of said NS5B.

12. (New) A method for identifying a HCV RNA-dependent RNA polymerase inhibitor comprising:

(a) incubating *in vitro* a composition comprising HCV NS5B, ribonucleotide substrates, an RNA template, and a test compound, under conditions suitable to produce NS5B RNA-dependent RNA polymerase activity in the absence of said compound; and

(b) measuring the ability of said compound to affect said NS5B RNA-dependent RNA polymerase activity.

13. (New) The method of claim 12, wherein said NS5B is the only HCV protein present during said incubating.

14. (New) The method of claim 12, wherein said method measures primer independent RNA-dependent RNA polymerase activity.

15. (New) The method of claim 13, wherein said method measures primer independent RNA-dependent RNA polymerase activity.

16. (New) The method of claim 12, wherein said NS5B is purified.

17. (New) The method of 12, wherein said NS5B has the amino acid sequence of SEQ ID NO:1.

18. (New) The method of claim 12, wherein said NS5B is produced from a NS2-NS3-NS4-NS5 polyprotein by means of multiple proteolytic events that occur in an organism expressing nucleic acid encoding said NS2-NS3-NS4-NS5 polyprotein, followed by purification of said NS5B.

19. (New) The method of claim 13, wherein said NS5B is provided as an extract of an organism expressing nucleic acid encoding said NS5B.

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REMARKS

The present application is amended by canceling claims 2-7, adding claims 8-12, referencing prior U.S. applications, and replacing the prior Sequence Listing. The enclosed sequence listing contains the same sequence information as the originally filed Sequence Listing. The enclosed Sequence Listing also updates the general information section and uses a different format to indicate sequence characteristics. No new matter was introduced into the enclosed Sequence Listing.

Accordingly the claims are in condition for allowance. Please charge deposit account 13-2755 for fees due in connection with this amendment. If any time extensions are needed for the timely filing of the present amendment, Applicants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

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